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Overview

Stroke and neuroplasticity

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Abstract

Stroke is one of the leading causes of mortality and disability in modern countries. Clinical manifestation of stroke is rapidly developing loss of brain function due to disturbance in the blood supply to the brain. Neuroplasticity, also known as cortical mapping, challenges the idea that brain functions are fixed in certain time. It refers to ability of the human brain to change as result of one's experience, that the brain is »plastic« and »flexible«. Neuroplasticity can act through two possible mechanisms on stroke disability-prevention and treatment of neurological deficit (cognitive impairment). Normal aging process and many different neurological disorders like stroke, dementia, Alzheimer's and Parkinson's disease, Huntington disease, multiple sclerosis and acquired brain trauma contribute to the decline of our cognitive abilities. Practicing mental stimulation improves memory and attention. The basis of the mental health is the control of conventional cerebrovascular risk factors, practice of physical activity, healthy nutrition, stress management and mental stimulation. Challenging the brain with different tasks creates new neural connections and intensive exercise leads to improvement in neuroplasticity.

INTRODUCTION

The brain damage caused by a stroke may result in the loss of cerebral function. However, the brain can use neuroplasticity to adjust itself functionally, by reorganizing the cortical maps, which contributes to the stroke recovery. The changes in the cortex organization include an increase in the number and density of dendrites, synapses and neurotrophic factors synthesis which results in two ways- unmasking of existing neuronal circuits and establishing of new neuronal circuits. Term neuroplasticity comes from greek word »plastos« which means pliable, it means that neurochemical, synaptical, receptor and functional reorganization in brain results in new functional possibilities.

After damage of the motor cortex, changes of activation in other motor areas are observed. These changes occur in homologue areas of the non-affected hemisphere which can substitute for the lost functions or in the intact cortex adjacent to the damage. Thanks to these cortical reorganizations, which begin from one to two days after the stroke, and can be extended for months, the patients can recover, at least in part, the lost abilities. The recovery of functions of the limbs which is promoted by plasticity is more difficult to occur, due to a phenomenon known as »learned non use«. With the loss of a brain area's function, the body part that was linked to this area is also affected and its mobility power is lost too. As the patient cannot move his most affected limb, he compensates this using the other limb. Thus, after a certain period, when the damage effects aren't present anymore and brain adaptations happen, the movements could be recovered, but the patient has already »learned« that the limb is no longer functional *(1)*.

Cognitive abilities like processing speed, memory and reasoning start to decline in our late twenties. Normal aging process and many different neurological disorders like stroke, dementia, Alzheimer's and Parkinson's disease, Huntington disease, multiple sclerosis and acquired brain trauma contribute to the decline of our cognitive abilities.

Mechanisms of neurodegeneration include tissue damage due to the failure of arterial circulation to bring oxygen or nutritive substances or due to the venous circulation failure to take away free radicals. It is known that increased neuronal activity requires more glucose and oxygen to be delivered rapidly through the blood stream. One of the consequences of normal aging is that the levels of the redox-active metals, copper and iron, in the brain increase which is more pronounced in neurodegenerative disorders. This increase could lead to hypermetallation of proteins that normally bind redox-active metals at shielded sites. It might also lead to the oxidative stress that is observed in neurodegenerative diseases. New research data cast the pericyte in a surprising new role as a key-player in shaping blood flow and in protecting sensitive brain tissue from harmful substances. Pericytes are uniquely positioned within the neurovascular unit and serve as vital integrators of angiogenesis, blood-brain barrier formation and maintenance, vascular stability and angioarchitecture, capillary blood flow regulation and regulation of toxic cellular byproducts clearance. Blood--brain barrier breakdown due to disruption of adherent junctions due to the perycites deficiency, leads to neuronal damage and neurodegeneration *(2)*. There are some evidences that inflammation has positive influence on neuroplasticity. There are evidences in animals whish proves that macrophages produces cytokines as well as growth factors which stimulates proliferation, differentiation and migration of cells (oligodendrocytes, mycroglia). These cells activates dopaminergic neurons thru glialderived neurothrophic factor (GDNF) and brain derived neurotrophic factor (BDNF). Neurotrophic factors (NF) produced in local immunological reactions have protective influence on neurons. One of the first and most famous neurotorphins is BDNF, it is responsible for long term memory, it prevents depressive mood disorders, it has positive influence on neurites and dendrites growth as well as increase in number of synapses and differentiation of steam cells also in adult brain. Neurodegeneration can be localized to the territory in case of acute accident in the territory of supplying vessel or diffuse in case of generalized blood supply insufficiency.

All these mechanisms can be visualized nowadays by mean of functional magentic resonance. It works in real time evaluating data about neuronal activity- it requires more glucose and oxygen to be delivered rapidly through the blood stream (hemodynamic response). Blood releases glucose to neurons and astrocytes at a greater rate than in the area of inactive neurons. Also, it results distinguishable change of the local ratio of oxyhemoglobin (diamagnetic; increases signal) to deoxyhemoglobin (paramagnetic;decreases signal). The magnetic resonance (MR) signal of blood is therefore slightly different depending on the level of oxygenation – BOLD (Blood--oxygen-level dependence), signal is composed of CBF contributions from larger arteries and veins.

THE BRAIN THAT CHANGES ITSELF

In 1868, French neurologist Jules Cotard had shown that children with a diseased left frontal lobe could speak quite well without it. These findings amount to the discovery that adult human brain, rather than being fixed or »hard-wired,« can not only change it, but it works by changing itself *(3)*. The invention of micromapping in the 1950's allowed neuroscientists to decode the communication of neurons *(4)*. Eminent neuroscientist Professor Michael M. Merzenich found that sensory and motor brain maps are not universal or immutable--they vary in their borders and size from person to person thus brain borders are blurrier than we ever imagined *(5)*. The brain is not hard-wired; new neural pathways can form through the end of life. Challenging the brain with different tasks creates new neural connections and intensive exercise leads to improvement in brain function *(6)*. In 1890. Wiliam James in his work »Principles of Psychology« introduced term neuroplasticity in psychiatry evaluating different mechanisms of adaptation in human psychological functioning. Santiago Ramon y Cahal used same principles in his observation of human psychology and underlying anatomical structures as well as functional changes in human brain.

There are few key principles of neural plasticity. The most popular ones are: »use it or lose it« and »use it and improve it« *(7–9)*. Also, the impuls must have some strictly defined characteristics: specificity, repetition, intensity, time (duration), salience, transference and interference as well as age of the individual.

Individuals who lead mentally stimulating lives, through education, occupation and leisure activities have reduced risk of developing dementia. In 1986, Italian neurologist Rita Levi-Montalcini and American biochemist Stanley Cohen identified set of proteins called nerve growth factors (NGF). Nerve growth factor affects neurons in particular, signaling certain types of cells to survive, to differentiate and grow *(10)*. BDNF acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support the survival of existing neurons and encourage the growth and differentiation of new neurons and synapses. In the brain, it is active in the hippocampus, cortex, and basal forebrain, areas vital to learning, memory, and higher thinking. Antidepressants intracellular sigma 1 receptors increase BDNF stimulated excitatory glutamatergic transmission (increased neuroplasticity).

Nowadays, computer assisted systems showed the promising results in brain challenging and stimulation. Systems are easy to use-little computer knowledge is necessary (point and click); stimulus is delivered accurately; performance gains are continuously tracked; task difficulty is in accordance with each user's progress; exercises are structured and complex *(11, 12)*. American neuroscientist Edward Taub has shown that paralysis caused by strokes; cerebral palsy, multiple sclerosis and brain trauma can be significantly improved using the interactive metronome-brain exercise that reorganizes the brain to work around dead tissue. In some cases, disabilities in place for as long as 50 years can be reversed. Constraint-induced movement therapy (CI-therapy) consists in the forced use of the affected arm by the limited use of the non-affected arm. During 10 to 15 days period, the patient's non-affected arm is immobilized. Due to this increased use of the affected arm, the brain area connected is stimulated again and an intense cortical reorganization occurs. Neuroplasticity is essential to the stroke patient's recovery, and one of the most effective methods used to stimulate it, is the CI-therapy, which have been achieving important results in the motor cortex reorganization and in getting over the »learned nonuse«. Another interesting device used in neuroplasticity process is so called »mirror box«. The patient places unaffected limb into one side of the box and the affected limb into the other side. Due to the mirror, the patient sees a reflection of the unaffected hand where the affected limb is placed. The patient thus receives artificial visual feedback that the affected limb is now moving when moving the unaffected hand *(13)*. American neuroscientist Paul Bach-y-Rita was one of the first to seriously study the idea of neuroplasticity (although it was first proposed in the late 19th century), and to introduce sensory substitution as a tool to treat patients suffering from neurological disorders. He invented another important device used in neuroplasticity evaluation-brain port. Brain Port is a device with integrated sensors which deliver fine-grained spatial information to the tongue and by extension to the brain. It is used in the cases of blindness (when the tongue is tapped, the regions of the brain associated with vision response) and as substitute for the vestibular apparatus (stimulation on the surface of the tongue was created by a dynamic pattern of electrical pulses and the patient was able to adjust the intensity of stimulation and spatially centralize the stimulus on the electrode array) *(14)*. The current research is taking two divergent pathways; it is oriented toward cognitive research (attention/concentration, language processing and academic fluency) and toward motor research (fine and gross motor skills, balance and gait).

PILLARS OF BRAIN HEALTH

Mainstay of the mental health is the control of the conventional cerebrovascular risk factors, practice of physical activity, and healthy nutrition, stress management and mental stimulation. Stress management is important, because stress has shown cytotoxic properties. Prolonged stress damages the hippocampus which is engaged in memory and learning. Practicing mental stimulation improves memory and attention. It also improves auditory processing (listening skills) and visual-spatial skills; word retrieval skills are improved as well as the speed of processing and concentration. The Nun Study revealed that higher education reduces dementia; diet and exercise were linked to healthy aging and longevity and that positive attitude decreased the risk of age-related problems *(9)*.

Recent data show that physical activity increases production of BDNF *(7)*. If its supply runs low, stress is not tolerated properly, and the brain is prone to inflammation, and cognitive decline. Physical exercise slows down age-related shrinkage of the frontal cortex which is responsible for executive function *(8)*. In 1999, researchers at the University of Illinois found that older people who started exercising showed faster reaction times, better ability to focus. In 2006, the same team found that aerobic exercisers actually increased their brain size by about 3%. In 2007, Columbia University researchers found that when people exercised regularly for three months, blood flow increased to a part of the hippocampus which is important for memory.

Mediteranian diet is the best for our brain and it has shown good results in prevention of cerebrovascular disease and neurodegeneratinon. The more colorful our diet is, the more antioxidants we get. Yellow/Orange: sweet potatoes, carrots, pumpkin, mango, corn, and melon all contain a variety of carotenoids. Green: spinach and broccoli are high in lutein. Blue/Purple: blueberries and blackberries are chock-full of anthocyanins. Red: tomatoes and watermelon are loaded with lycopene. White: cauliflower offers the same cancer-fighting benefits as broccoli, and potatoes are a good source of vitamin C. Garlic and onions have also antioxidants. Pretreatment of experimental animals with with either blueberry, spinach, or spirulina enriched diets significantly reduced the cortical infarction induced by middle cerebral artery occlusion/reperfusion *(15, 16)*.

However, common tips for maintaining brain health include: keeping the emotional connections with family and friends, developing stimulating friendships, continually exposing to new stimulating activities and always trying getting out of the comfort zone.

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